

## BIOGRAPHICAL SKETCH

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NAME  Beatrice H. Hahn, M.D.  eRA COMMONS USER NAME bhahn@uab.edu	POSITION TITLE  Professor of Medicine and Microbiology		

EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.*)

INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
University of Munich, Germany	M.D.	1981	Medicine
University of Munich, Germany	Intern	1981-1982	Medicine
National Cancer Institute, Bethesda, MD	Postdoc	1982-1985	Human Retrovirology

### A. Personal Statement

My laboratory has a long-standing interest in elucidating the origins and evolution of human and simian immunodeficiency viruses and in studying HIV/SIV gene function and disease mechanisms from an evolutionary perspective. We were the first to describe the extensive *in vivo* genetic variability of HIV-1 (Hahn et al., *PNAS*, 1985; Shaw et al., *Science*, 1985) and discovered that recombination between highly divergent viruses represents a major driving force of HIV/SIV diversification (Robertson et al., *Nature*, 1995; Sharp et al., *Nature*, 1996). We also developed methods for non-invasive SIV detection and molecular characterization in wild-living apes (Santiago et al., *Science*, 2002; Keele et al., *Science* 2006), which led to the identification of the chimpanzee reservoirs of pandemic (group M) and non-pandemic (group N) HIV-1 (Gao et al., *Nature* 1999, Keele et al., *Science*, 2006). More recently, we have characterized HIV-1 transmission at the molecular level, developing theoretical frameworks that permit the identification and enumeration of transmitted founder (TF) HIV-1 and SIV strains (Salazar et al., *J Virol*, 2008; Keele et al., *PNAS*, 2008; Lee et al., *J Theor Biol*, 2009; Keele et al., *J. Exp. Med.*, 2009). In this context, a key technical innovation was the application of single genome sequencing (SGS) to derive HIV/SIV amplicons from heterogeneous templates without PCR artifacts. We also developed effective strategies to clone TF and chronic control viral genomes for biological testing (Salazar et al., *J. Exp. Med.*, 2009; Li et al., *PLoS Pathogens*, 2010; Wilen et al., *J Virol*, 2011, Parrish et al., *PLoS Pathogens*, 2012) and identified, enumerated, and characterized TF genomes from injection drug users, so that direct comparisons between viruses transmitted by mucosal and intravenous routes could be made (Bar et al., *J Virol*, 2010). These innovations have yielded panel of well-characterized infectious molecular clones (IMCs) as well as a first understanding of the earliest virus - host interactions that underlie mucosal transmission. The latter included the unexpected discovery that that viruses that have successfully crossed the mucosa are considerably more resistant to the antiviral effects of type 1 interferons (IFNs) than viruses that predominate during chronic infection (Parrish et al., *PNAS*, 2013; Fenton-May et al., *Retrovirology*, 2013). In collaboration with Persephone Borrow, who will serve as the Co-Principal Investigator and provide important immunological expertise, we propose to further dissect these early protective host effector activities and potentially harness them for novel anti-HIV-1 interventions.

### B. Positions and Honors

#### Positions and Employment

1974-1976	Medical School, University of Regensburg, Germany (basic sciences)
1976-1981	Medical School, University of Munich, Germany (clinical sciences)
1976-1980	Doctoral thesis, University of Munich, Germany
1981-1982	Internship, Department of Internal Medicine, University of Munich, Germany
1982-1985	Postdoctoral Fellow, Laboratory of Tumor Cell Biology (Mentor: R.C. Gallo), NCI, NIH
1985-1987	Asst. Professor, Depts. of Medicine (Div. of Hematology/Oncology) & Microbiology, UAB
1988-1992	Assoc. Prof., Depts. of Medicine (Div. of Hematology/Oncology) & Microbiology, UAB
1992- 2011	Professor, Depts. of Medicine (Div. of Hematology/Oncology) & Microbiology, UAB
2011- present	Professor, Depts. of Medicine (Div. of Hematology/Oncology) & Microbiology, University of Pennsylvania (U Penn)

## **Other Experience and Honors**

1986	Special Fellow, Leukemia Society of America
1987	Junior Faculty Developmental Award, University of Alabama at Birmingham
2001	Recipient, The Max Cooper Award for Research Excellence
2002	"The 50 Most Important Women in Science", <i>Discover Magazine</i>
1994-2004	100 Most Cited Scientists in Microbiology ( <a href="http://www.in-cites.com">http://www.in-cites.com</a> )
2004-present	Editor, Journal of Virology
2005	Recipient, Bristol-Myers Squibb <i>Freedom to Discover Award</i> (Infectious Diseases)
2007	<i>Neal Nathanson Lectureship</i> , University of Pennsylvania School of Medicine
2009	<i>Harold C. Neu Lecture and Visiting Professorship</i> , Columbia University.
2009	<i>Merle Sande Memorial Lecture</i> , The Gladstone Institute of Virology and Immunology
2010	<i>John T. Carey Lectureship</i> , Case Western Reserve University
2010	<i>Evers Lecturer in Infectious Diseases</i> , New York University School of Medicine
2010	<i>Norman P. Salzman Memorial Award and Lecture in Virology</i> , NIH
2012	<i>Bernard Fields Lecture on Microbial Pathogenesis</i> , Scripps Research Institute
2012	<i>Dean's Distinguished Lecturer</i> , University of Colorado
2012	<i>Rosalind Franklin Lecturer</i> , King's College London

## **Professional Memberships**

1993	Member, American Society for Clinical Investigation
2000	Member, American Association of Physicians
1997-2002	Member, Board of Scientific Counselors, National Cancer Institute
1996-2003	Member, National Institutes of Health AIDS Vaccine Research Committee
2010	Fellow, American Academy of Microbiology
2010	Member, Institute of Medicine of the National Academies (IOM).
2012	Member, National Academy of Sciences (NAS)

## **C. Selected Peer-reviewed Publications** (selected from over 300 peer-reviewed publications)

### **Most relevant to the current application**

1. Salazar-Gonzalez J.F., Bailes E., Pham K.T., Salazar M.G., Guffey M.B., Keele B.F., Derdeyn C.A., Farmer P., Hunter E., Allen S., Manigart O., Mulenga J., Anderson J.A., Swanstrom R., Haynes B.F., Athreya G.S., Korber B.T., Sharp P.M., Shaw G.M., **Hahn B.H.** (2008) Deciphering human immunodeficiency virus type 1 transmission and early envelope diversification by single-genome amplification and sequencing. *J. Virol.* 82: 3952-3970. PMCID: PMC2293010
2. Keele, B.F., Giorgi, E.E., Salazar-Gonzalez, J.F., Decker, J.M., Pham, K.T., Salazar, M.G., Sun, C., Grayson, T., Wang, S., Li, H., Wei, X., Jiang, C., Kirchherr, J.L., Gao, F., Anderson, J.A., Ping, L-H., Swanstrom, R., Tomaras, G.D., Blattner, W.A., Goepfert, P.A., Kilby, J.M., Saag, M.S., Delwart, E.L., Busch, M.P., Cohen, M.S., Montefiori, D.C., Haynes, B.F., Gaschen, B., Athreya, G.S., Lee, H.Y., Wood, N., Seoighe, C., Perelson, A.S., Bhattacharya, T., Korber, B.T., **Hahn, B.H.**, and Shaw, G.M. (2009) Identification and characterization of transmitted and early founder virus envelopes in primary HIV-1 infection. *PNAS* 105:7552-7557, 2008. PMCID: PMC2387184
3. Keele, B.F., Li, H., Learn, G.H., Hraber, P., Giorgi, E.E., Grayson, T., Sun, C., Chen, Y., Yeh, W.W., Letvin, N.L., Mascola, J.R., Nabel, G.J., Haynes, B.F., Bhattacharya, T., Perelson, A.S., Korber, B.T., **Hahn, B.H.** and Shaw, G.M. (2009) Low dose rectal inoculation of Rhesus Macaques by SIVsmE660 or SIVmac251 recapitulates human mucosal infection by HIV-1. *J. Exp. Med.* 206:1117-1134. PMCID: PMC2715022
4. Salazar-Gonzalez, J.F., Salazar, M.G., Keele, B.F., Learn, G.H., Giorgi, E.E., Li, H., Decker, J.M., Wang, S., Baalwa, J., Kraus, M.H., Parrish, N.F., Shaw, K.S., Guffey, M.B., Bar, K.J., Davis, K.L., Ochsenbauer-Jambor, C., Kappes, J.C., Saag, M.S., Cohen, M.S., Mulenga, J., Derdeyn, C.A., Allen, S., Hunter, E., Markowitz, M., Hraber, P., Perelson, A.S., Bhattacharya, T., Haynes, B.F., Korber, B.T., **Hahn, B.H.**, and Shaw, G.M. (2009) Genetic identity, biological phenotype and evolutionary pathways of transmitted/founder viruses in acute and early HIV-1 infection. *J. Exp. Med.* 206:1273-1289. PMCID: PMC2715054

5. Lee H.Y., Giorgi E.E., Keele B.F., Gaschen B., Athreya G.S., Salazar-Gonzalez J.F., Pham K.T., Goepfert P.A., Kilby J.M., Saag M.S., Delwart E.L., Busch M.P., **Hahn B.H.**, Shaw G.M., Korber B.T., Bhattacharya T., Perelson A.S. (2009) Modeling sequence evolution in acute HIV-1 infection. *J Theor Biol* 261(2): 341-360. PMCID: PMC2760689
6. Li, H., Bar, K.J., Wang, S., Decker, J.M., Chen, Y., Sun, C., Salazar-Gonzalez, J.F., Salazar, M.G., Learn, G.H., Morgan, C.J., Schumacher, J.E., Hraber, P., Giorgi, E.E., Bhattacharya, T., Korber, B.T., Perelson, A.S., Eron, J.J., Cohen, M.S., Hicks, C.B., Haynes, B.F., Markowitz, M., Keele, B.F., **Hahn, B.H.**, and Shaw, G.M. (2010). High multiplicity infection by HIV-1 in men who have sex with men. *PLoS Pathog.* e1000890. PMCID: PMC2869329
7. Fischer W., Ganusov V.V., Giorgi E.E., Hraber P.T., Keele B.F., Leitner T., Han C.S., Gleasner C.D., Green L., Lo C.C., Nag A., Wallstrom T.C., Wang S., McMichael A.J., Haynes B.F., **Hahn B.H.**, Perelson A.S., Borrow P., Shaw G.M., Bhattacharya T., Korber B.T. (2010) Transmission of single HIV-1 genomes and dynamics of early immune escape revealed by ultra-deep sequencing. *PLoS One* 5(8): e12303. PMCID: PMC2924888
8. Wilen, C.B., Parrish, N.F., Pfaff, J.M., Decker, J.M., Henning, E.A., Haim, H., Petersen, J.E., Wojcechowskyj, J.A., Sodroski, J.S., Haynes, B.F., Montefiori, D.C., Tilton, J.C., Shaw, G.M., **Hahn, B.H.**, and Doms, R.W. (2011) Phenotypic and immunologic comparison of clade B transmitted/founder and chronic HIV-1 envelope glycoproteins. *J. Virol.* 85:8514-8527. PMCID: PMC31658206
9. Gnanakaran, S., Bhattacharya, T., Daniels, M., Keele, B.F., Hraber, P., Lapedes, A., Shen, T., Gaschen, B., Krishnamoorthy, M., Li, H., Decker, J.M., Salazar-Gonzalez, J.F., Wang, S., Jiang, C., Gao, F., Swanstrom, R., Anderson, J.A., Ping, L-H., Cohen, M.S., Markowitz, M., Goepfert, P.A., Saag, M.S., Eron, J.J., Hicks, C.B., Blattner, W.A., Tomaras, G.D., Asmal, M., Letvin, N.L., Gilbert, P.B., DeCamp, A.C., Magaret, C.A., Schief, W.R., Ban Y.A., Zhang, M., Soderberg, K.A., Sodroski, J.G., Haynes, B.F., Shaw, G.M., **Hahn, B.H.** and Korber, B.T. (2011) Recurrent signature patterns in HIV-1 B clade envelope glycoproteins associated with either early or chronic infections. *PLoS Pathog.* 7:e1002209. PMCID: PMC3182927
10. Parrish, N. F., Wilen C. B., Banks L. B., Iyer S. S., Pfaff J. M., Salazar-Gonzalez J. F. , Salazar M. G., Decker J. M., Parrish E. H., Berg A., Hopper J., Hora B., Kumar A., Mahlokozera T., Yuan S., Coleman C., Vermeulen M., Ding H., Ochsenbauer C., Tilton J. C., Permar S. R., Kappes J. C., Betts M. R., Busch M. P., Gao F., Montefiori D., Haynes B. F., Shaw G. M., **Hahn B. H.**, and Doms R. W. (2012) Transmitted/founder and chronic subtype C HIV-1 use CD4 and CCR5 receptors with equal efficiency and are not inhibited by blocking the integrin  $\alpha 4\beta 7$ . *PLoS Path.* 8:e1002686. PMCID: PMC3364951
11. Baalwa, J., Wang S., Parrish N. F., Decker J. M., Keele B. F., Learn G. H., Yue L., Ruzagira E., Ssemwanga D., Kamali A., Amornkul P. N., Price M. A., Kappes J. C., Karita E., Kaleebu P., Sanders E., Gilmour J., Allen S., Hunter E., Montefiori D. C., Haynes B. F., Cormier E., **Hahn B. H.**, and Shaw G. M. (2013) Molecular identification, cloning and characterization of transmitted/founder HIV-1 subtype A, D and A/D infectious molecular clones. *Virology* 436:33-48, 2013. PMCID: PMC3545109
12. Parker, Z. F., Iyer S. S., Wilen C. B., Parrish N. F., Chikere K. C., Lee F.H., Didigu C. A., Berro R., Klasse P. J., Lee B., Moore J. P., Shaw G. M., **Hahn B. H.**, and Doms R. W. (2012) Transmitted/founder and chronic HIV-1 envelope proteins are distinguished by differential utilization of CCR5. *J. Virol* 87:2401-11, 2013. PMCID: PMC3571396
13. Parrish, N.F., Gao, F., Li, H., Giorgi, E.E., Barbian, H.J., Parrish, E.H., Zajic, L., Iyer, S.S., Decker, J.M., Kumar, A., Hora, B., Berg, A., Cai, F., Hopper, J., Denny, T.N., Ding, H., Ochsenbauer, C., Kappes, J.C., Galimidi, R.P., West, A.P., Bjorkman, P.J., Wilen, C.B., Doms, R.W., O'Brien, M., Bhardwaj, N., Borrow, P., Haynes, B.F., Muldoon, M., Theiler, J.P., Korber, B., Shaw, G.M., and **Hahn, B.H.** (2013) Phenotypic properties of transmitted founder HIV-1. *PNAS* 110:6626-33. PMCID: PMC3637789
14. Liao, H.-X., Lynch, R., Zhou, T., Gao, F., Alam, M., Boyd, S., Fire, A., Roskin, K.M., Schramm, C.A., Zhang, Z., Zhu, J., Shapiro, L., Mullikin, J.C., Gnanakaran, G., Hraber, P., Wiehe, K., Kelsoe, G., Yang, G., Xia, S.-M., Montefiori, D.C., Parks, R., Lloyd, K.E., Scearce, R.M., Soderberg, K.D., Cohen, M., Kaminga, G., Louder, M., Tran, L., Chen, Y., Cai, F., Chen, S., Moquin, S., Du, X., Joyce, M.G., Srivatsan, S., Zhang, B., Zheng, A., Shaw, G.M., **Hahn, B.H.**, Kepler, T.B., Korber, B.T., Kwong, P.D., Mascola, J.R., and Haynes, B.F. (2013) Co-evolution of a broadly neutralizing HIV-1 antibody and founder virus. *Nature* 496:469-76. PMCID: PMC3637846

15. Fenton-May, A.E., Dibben, O., Emmerich, T., Ding, H., Pfafferott, K. Aasa-Chapman, M.M., Pellegrino, P., Williams, I., Cohen, M.S., Gao, F., Shaw, G.M., **Hahn, B.H.**, Ochsenbauer, C., Kappes, J.C., and Borrow, P. Relative resistance of HIV-1 founder viruses to control by interferon-alpha. *Retrovirology* 10:146, 2013. [Epub ahead of print]

#### D. Research Support (Active)

##### **R37 AI50529 (Hahn)**

**08/01/01 - 01/31/18**

National Institutes of Health/NIAID

##### *Natural SIV Reservoirs and Human Zoonotic Risk*

This grant focuses on the characterization of natural SIV reservoirs and associated human zoonotic risk. Specifically, we will (i) identify the ape reservoirs of HIV-1 groups O and P, (ii) determine the natural history of SIVgor infection, (iii) determine whether wild apes serve as a recurrent source for human infection and (iv) identify viral determinants of cross-species transmission and human adaptation.

##### **R01 AI058715 (Hahn)**

**04/01/04 – 06/30/14**

National Institutes of Health/NIAID

##### *Molecular Epidemiology and Natural History of SIVcpz*

This grant is focused on conducting natural history studies of SIVcpz infection in wild chimpanzees in Gombe National Park. Specifically, we will (i) monitor SIVcpz prevalence and incidence rates, (ii) identify viral and host determinants of SIVcpz pathogenicity, and (iii) determine if co-infections by other pathogens influence SIVcpz morbidity and mortality.

##### **R01 AI091595 (Hahn)**

**09/20/11 – 08/31/14**

National Institutes of Health/NIAID

##### *Great Ape Reservoirs of Human Malaria*

Malaria is one of the most devastating infectious diseases in the world and one of the major global public health problems. This application will identify and molecularly characterize all *Plasmodium* species that infect chimpanzees, gorillas and bonobos in the wild, and determine whether these apes serve as a recurrent source for human infections.

##### **UM1 AI100645 (Haynes)**

**07/1/12 - 06/30/19**

National Institutes of Health/NIAID

##### *Center for HIV/AIDS Vaccine Immunology and Immunogen Discovery (CHAVI-ID)*

##### *Virus Biology Research Support Component*

Dr. Hahn directs the Virus Biology SRSC, which provides state-of-the-art molecular approaches, reagents and service to CHAVI-ID investigators by identifying specific sites and mechanisms of interception in the HIV-1 transmission process. Specifically, the Virus Biology SRSC will explore the impact of Env quasispecies evolution on the development of broadly neutralizing antibodies.

##### **P01 AI088564 (Shaw)**

**07/15/10 – 06/30/15**

National Institutes of Health/NIAID

##### *Novel SIVsmm Strains for Analysis of Mucosal Transmission and Vaccine Protection*

This application will identify, molecularly clone, and in vivo analyze naturally-occurring mucosally-transmitted strains of SIVsmm to reveal viral-host interactions responsible for selective SIV transmission across rectal, vaginal and cervical mucosa and will provide novel, genetically-divergent, pathogenic virus challenge strains for vaccine testing. Dr. Hahn leads Project #2 in this program project